

**RECEIVED**  
**CENTRAL FAX CENTER**Serial No. 10/750,934  
Docket No. 0101.00**MAR 25 2008**Claims:

The following listing of claims will replace all prior versions and listings of claims in the application:

1 - 22. (Cancel)

23. (Withdrawn) A method of making a pharmaceutical formulation for pulmonary administration, the method comprising: suspending active agent particles and a hydrophobic material in a liquid feedstock, wherein at least 90% of the active agent particles have a geometric diameter less than 3  $\mu\text{m}$ ; and spray drying the feedstock suspension to produce particulates comprising an active agent particle at least partially in the hydrophobic material.

24. (Withdrawn) A method according to claim 23 wherein the feedstock comprises water and wherein the active agent has a solubility in water of less than 1.0 mg/ml.

25. (Withdrawn) A method according to claim 23 further comprising collecting the particulates.

26. (Withdrawn) A method according to claim 25 wherein the collected particulates have a mass median diameter less than 20  $\mu\text{m}$ .

27. (Withdrawn) A method according to claim 25 wherein the collected particulates have a mass median diameter less than 10  $\mu\text{m}$ .

28. (Withdrawn) A method according to claim 23 wherein 95% of the active agent particles have a geometric diameter less than 3  $\mu\text{m}$ .

29. (Withdrawn) A method according to claim 23 wherein the hydrophobic material comprises a lipid.

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30. (Withdrawn) A method according to claim 23 wherein the hydrophobic material comprises a phospholipid.

31. (Withdrawn) A method according to claim 23 wherein the hydrophobic material comprises a hydrophobic amino acid.

32. (Withdrawn) A method according to claim 23 further comprising adding an emulsifying agent to the feedstock.

33. (Withdrawn) A method according to claim 23 wherein the emulsifying agent comprises distearoyl phosphatidylcholine.

34. (Withdrawn) A method according to claim 23 further comprising adding a blowing agent to the feedstock.

35. (Withdrawn) A method according to claim 23 further comprising adding a polyvalent cation to the feedstock.

36. (Withdrawn) A method according to claim 23 wherein the feedstock is spray dried in a manner to produce particulates having a bulk density of less than  $0.5 \text{ g/cm}^3$ .

37. (Withdrawn) A pharmaceutical formulation prepared by a method according to claim 23.

38. (Currently Amended) A pharmaceutical formulation for pulmonary administration, the pharmaceutical formulation comprising:

porous particulates consisting essentially of active agent particles in a matrix comprising a phospholipid, the active agent particles having a geometric diameter of less than about  $3 \mu\text{m}$  and a solubility in water of less than about 0.1 to about 1.0 mg/ml and wherein the active agent particles are dispersed ~~throughout~~ within the phospholipid matrix; and

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~~wherein at least 90% of the active agent particles have a geometric diameter less than 3  $\mu\text{m}$  and~~ wherein the particulates are hollow and/or porous, and have a mass median diameter less than 20  $\mu\text{m}$ , a bulk density of less than about 0.5 g/cm<sup>3</sup> and a mass median aerodynamic diameter less than about 2.6  $\mu\text{m}$ .

39. (Previously Presented) A pharmaceutical formulation according to claim 38 wherein the formulation provides for the delivery to the lung of a dose of at least about 5 mg in a single inhalation.

40. (Cancel)

41. (Previously Presented) A pharmaceutical formulation according to claim 38 wherein a formulation fine particle fraction of less than 3.3  $\mu\text{m}$  is at least about 72 percent.

42. (Previously Presented) A pharmaceutical formulation according to claim 38 wherein the formulation provides for the delivery to the lung of a dose of at least about 5 mg in a single inhalation.

43. (Cancelled).

44. (Previously Presented) A pharmaceutical formulation according to claim 38 wherein the matrix comprises one or more of dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, diarachidoylphosphatidylcholine, dibehenoylphosphatidylcholine, diphosphatidyl glycerol, short-chain phosphatidylcholines, long-chain saturated phosphatidylethanolamines, long-chain saturated phosphatidylserines, long-chain saturated phosphatidylglycerols, and long-chain saturated phosphatidylinositols.

45-46. (Cancelled)

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47. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates have a bulk density less than  $0.3 \text{ g/cm}^3$ .
48. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates have a bulk density less than  $0.2 \text{ g/cm}^3$ .
49. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates are in dry powder form for aerosolization in a dry powder inhaler.
50. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates are suspended in a propellant for aerosolization in a metered dose inhaler.
51. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates are suspended within a liquid for aerosolization in a nebulizer.
52. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates further comprise a polyvalent cation.
53. (Previously Presented) A pharmaceutical formulation according to claim 38 wherein the particulates are formed by spray drying with a blowing agent.
54. (Currently Amended) A pharmaceutical formulation for pulmonary administration, the pharmaceutical formulation comprising:  
particulates ~~comprising~~ consisting essentially of amphotericin B ~~particle~~ particles in a matrix comprising a phospholipid wherein the amphotericin B particles have a solubility in water of ~~less than~~ about 0.1 to about 1.0 mg/ml, and are dispersed ~~throughout~~ within the phospholipid matrix, and;  
wherein the particulates are ~~hollow and/or~~ porous and have a mass median diameter less than  $20 \text{ }\mu\text{m}$ , a bulk density of less than about  $0.5 \text{ g/cm}^3$  and a mass median aerodynamic diameter less than about  $2.6 \text{ }\mu\text{m}$ .

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55. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a mass median diameter less than 10  $\mu\text{m}$ .
56. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a mass median diameter less than 5  $\mu\text{m}$ .
57. (Cancelled) A pharmaceutical formulation according to claim 54 wherein at least some of the particulates comprise a plurality of amphotericin B particles in a lipid matrix.
58. (Original) A pharmaceutical formulation according to claim 54 wherein the amphotericin B particles are crystalline.
59. (Cancelled)
60. (Previously Presented) A pharmaceutical formulation according to claim 54 wherein the lipid matrix comprises one or more of dipalmitoylphosphatidylcholine, distearoylphosphatidylcholine, diarachidoylphosphatidylcholine, dibehenoylphosphatidylcholine, diphosphatidyl glycerol, short-chain phosphatidylcholines, long-chain saturated phosphatidylethanolamines, long-chain saturated phosphatidylserines, long-chain saturated phosphatidylglycerols, and long-chain saturated phosphatidylinositols.
61. (Cancelled)
62. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a bulk density less than 0.3 g/cm<sup>3</sup>.
63. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a bulk density less than 0.2 g/cm<sup>3</sup>.

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64. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates are in dry powder form for aerosolization in a dry powder inhaler.

65. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates are suspended in a propellant for aerosolization in a metered dose inhaler.

66. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates are suspended within a liquid for aerosolization in a nebulizer.

67. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates further comprise a polyvalent cation.

68. (Previously Presented) A pharmaceutical formulation according to claim 54 wherein the particulates are formed by spray drying with a blowing agent.

69 – 83. (Cancelled).

84. (Withdrawn) A method of making a pharmaceutical formulation for pulmonary administration, the method comprising: suspending amphotericin B particles and a hydrophobic material in a liquid feedstock, wherein at least 90% of the active agent particles have a geometric diameter less than 3  $\mu\text{m}$ ; and spray drying the feedstock suspension to produce particulates comprising amphotericin B at least partially in the hydrophobic material.

85. (Withdrawn) A method according to claim 84 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 20  $\mu\text{m}$ .

86. (Withdrawn) A method according to claim 84 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 10  $\mu\text{m}$ .

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87. (Withdrawn) A method according to claim 84 wherein the hydrophobic material comprises a lipid.
88. (Withdrawn) A method according to claim 84 wherein the hydrophobic material comprises a phospholipid.
89. (Withdrawn) A method according to claim 84 wherein the hydrophobic material comprises a hydrophobic amino acid.
90. (Withdrawn) A method according to claim 84 further comprising adding an emulsifying agent to the feedstock.
91. (Withdrawn) A method according to claim 84 further comprising adding a blowing agent to the feedstock.
92. (Withdrawn) A method according to claim 84 further comprising adding a polyvalent cation to the feedstock.
93. (Withdrawn) A method according to claim 84 wherein the feedstock is spray dried in a manner to produce particulates having a bulk density of less than  $0.5 \text{ g/cm}^3$ .
94. (Withdrawn) A pharmaceutical formulation prepared by a method according to claim 84.
95. (Withdrawn) A method of making a pharmaceutical formulation for pulmonary administration, the method comprising: suspending amphotericin B particles in a liquid feedstock, the liquid feedstock having a lipid and a blowing agent dissolved or suspended therein; and spray drying the feedstock suspension to produce hollow and/or porous particulates comprising amphotericin B and the lipid.

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96. (Withdrawn) A method according to claim 95 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 20  $\mu\text{m}$ .

97. (Withdrawn) A method according to claim 95 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 10  $\mu\text{m}$ .

98. (Withdrawn) A method according to claim 95 wherein the lipid comprises a phospholipid.

99. (Withdrawn) A method according to claim 95 further comprising adding an emulsifying agent to the feedstock.

100. (Withdrawn) A method according to claim 95 further comprising adding a polyvalent cation to the feedstock.

101. (Withdrawn) A method according to claim 95 wherein the feedstock is spray dried in a manner to produce particulates having a bulk density of less than 0.5 g/cm<sup>3</sup>.

102. (Withdrawn) A pharmaceutical formulation prepared by a method according to claim 95.

103. (Currently Amended) A pharmaceutical formulation according to claim [[1]] 38 wherein the active agent comprises ciprofloxacin.

104. (New) A particulate pharmaceutical formulation in dry powder form for aerosolization and pulmonary administration, which comprises

an active agent particle having a geometric diameter of less than about 3  $\mu\text{m}$  and at least one property of a solubility in water of about 0.1 to about 1.0 mg/ml, or a low glass transition temperature;



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a porous phospholipid material matrix of surrounding the active agent particle wherein the active agent particle is substantially within the phospholipid matrix; and wherein the particulate pharmaceutical formulation is formed by preparing a feedstock comprising a suspension of the active agent particles and the phospholipid material, and spray-drying the feedstock to produce porous particulates having a mass median diameter less than 20  $\mu\text{m}$ , a bulk density of less than about 0.5  $\text{g}/\text{cm}^3$  and a mass median aerodynamic diameter less than about 2.6  $\mu\text{m}$ .

105. (New) The pharmaceutical formulation according to claim 104 wherein the particulates have a bulk density less than 0.3  $\text{g}/\text{cm}^3$ .

106. (New) The pharmaceutical formulation according to claim 104 wherein the low glass transition temperature comprises about 283°C.